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“Inner GPS”, a far-reaching influence in brain research —For the Nobel Prize in Physiology or Medicine 2014

HE RongQiao

State Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China

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On the day of Oct. 6, 2014, John O’Keefe and a Norwegian couple May-Britt Moser and Edvard Moser won the Nobel Prize in Physiology or Medicine for discovering the “inner GPS” that functions in the brain when the animals navigate through the world. The prize was awarded for their work in identifying the cells that make up the positioning system in the mammalian brain.

Hippocampal “place cells” are presumably the principal cells in each of the layers that fire in complex bursts when an animal moves through a specific location. In 1971, by recording electrophysiological signals, O’Keefe discovered the “place cells” in the rat hippocampus and proposed that the hippocampus functions as a cognitive map for spatial memory [1]. He observed that place cells spike at different phases relative to theta rhythm oscillations in hippocampal local field potential. As a rat enters the firing field of a place cell, the spiking starts during late phases of the theta rhythm, and as the rat moves through the firing field, the spikes shift to earlier phases of the theta cycle (http://en.wikipedia.org/wiki/John_O’Keefe_(neuroscientist)). This effect has been replicated in numerous other laboratories, providing evidence for the coding of sensory input by the timing of spikes. Thus, evidence from place cells offers strong support for hippocampal involvement in spatial mapping [2].

Through the 1980s and 1990s, the prevailing theory was that the formation of place fields originated within the hippocampus itself (Scientific Background-Nobelprize.org). In 2002, May-Britt and Edvard Moser found that disconnecting projections from the entorhinal cortex through the CA3 did not abolish the CA1 place fields [3]. In a later study using larger arenas for the animals to move in, they discovered a novel neuronal cell type, the “grid cell,” with unusual properties [4].

The grid cell generates a coordinate system for precise positioning and pathfinding. The Mosers’ study demonstrated that grid cells in the rat entorhinal cortex help animals to understand where they are [5]. They inserted electrodes into the rat entorhinal cortex and recorded electrical signals from individual grid cells as the rat ran around a box eating chocolate treats. A single grid cell fired when the rat crossed certain points on the floor; it turns out that these points formed a hexagonal grid, similar to a honeycomb. Results showed that each cell generates its own grid, and these overlapping patterns help the rat to recognize its location and direction. These discoveries have not only provided a better understanding of brain function in navigation, but have also opened novel avenues for studying cognitive functions (http://en.wikipedia.org/wiki/Grid_cell).

The visual orientation columns are organized regions of neurons, which are excited by visual line stimuli of varying angles that are located in the primary visual cortex and span multiple cortical layers. The geometry of the orientation columns are arranged in slabs that are perpendicular to the surface of the primary visual cortex [6]. For visual orientation, animals and humans create a typical ordinate with neurons in a quadrate (90°) pattern (Figure 1A) in the primary visual cortex, but a hexagonal (120°) pattern with six triangles in the entorhinal cortex (Figure 1B). Does the

email: herq@sun5.ibp.ac.cn

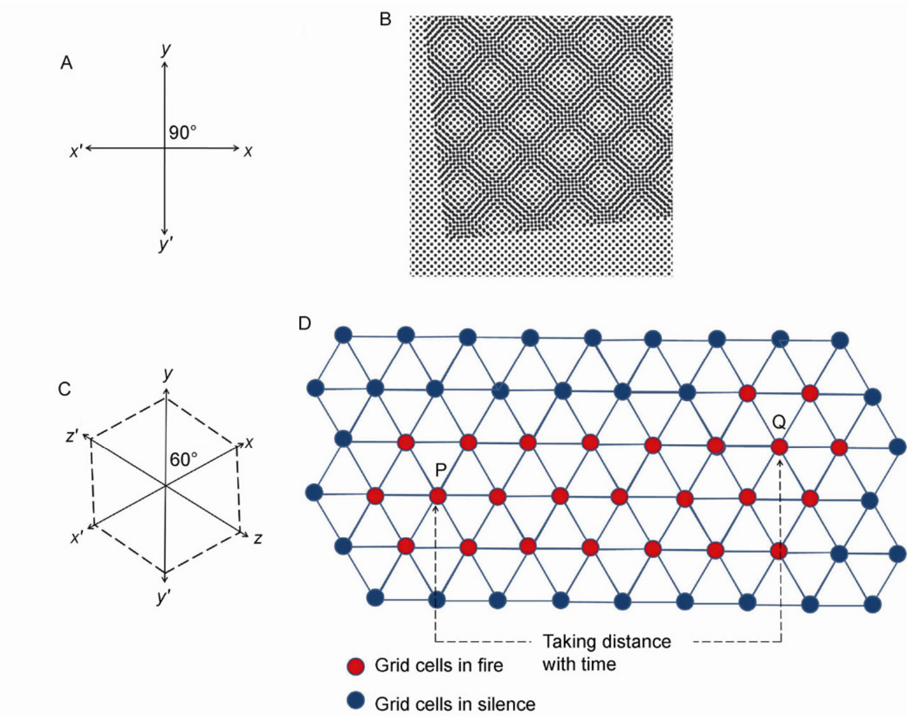

Figure 1 Quadrant and hexagonal coordinates, as well as displacement with time. Classical quadrant coordinates (A) and visual orientation columns (B, an example of a Moiré interference pattern [7]), hexagonal entorhinal coordinate (C), and displacement with time (D). What is the relationship between quadrant and hexagonal coordinates? What collaborates with the hippocampus and entorhinal cortex for brain to perceive navigation and passing of time, e.g., distance, time, and velocity? Where is the collaborator located in the brain?

hexagonal pattern give a higher-possible spatial resolution with fewer neurons than a quadrate or other patterns? What is the relationship between the quadrate and hexagonal patterns? Furthermore, when a rat moves from A to B, the animal will need a certain amount of time. What brain region cooperatively perceives the time (Figure 1C), and calculates the distance, time, and velocity? Future studies are still needed to answer these questions.

The knowledge about the brain's positioning system may help to better understand the mechanism underpinning the devastating spatial memory loss that affects individuals with Alzheimer's disease. Their work provides the possibility to further investigate why and how Alzheimer's disease selectively impairs the positioning system in humans. Many of the anatomical structures implicated in visiospatial attention function supramodally and are also involved with audiospatial attention. The cognitive consequences of this connection, which may be related to multimodal processing, have yet to be fully explored.

O'Keefe and the Mosers' work may provide insight into the relationship between visiospatial and audiospatial navigation. Their achievements will encourage scientists to investigate the role of the spatial navigation system in other positioning systems, such as auditory and olfactory perceptions. The Mosers' work has also provided traction for one of the most challenging research frontiers: how the brain computes. Their work helped to clarify the codes that allow for the animal brain to represent features of the external world (such as sound, smell, and position in space). Can their findings be used as a reference or model system to study and design artificial intelligence?

1 O'Keefe J, Dostrovsky J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. Brain Res, 1971, 34: 171–175
2 O'Keefe J, Nadel L. The Hippocampus as a Cognitive Map. Oxford: Oxford University Press, 1978
3 Brun VH, Otnass MK, Molden S, Steffenach HA, Witter MP, Moser MB, Moser EI. Place cells and place recognition maintained by direct entorhinal-hippocampal circuitry. Science, 2002, 296: 2243–2246
4 Hafting T, Fyhn M, Molden S, Moser MB, Moser EI. Microstructure of a spatial map in the entorhinal cortex. Nature, 2005, 436: 801–806
5 Fyhn M, Molden S, Witter MP, Moser EI, Moser MB. Spatial representation in the entorhinal cortex. Science, 2004, 305: 1258-1264
6 Hubel DH, Wiesel TN. Sequence regularity and geometry of orientation columns in monkey striate cortex. J Comp Neurol, 1974, 158: 267–294
7 Paik S, Ringach DL. Retinal origin of orientation maps in the visual cortex. Nat Neurosci, 2011, 14: 919–925